REMARKS/ARGUMENTS:

New claims 74-83 have been added to more specifically set forth certain aspects of the invention. Claims 74-83 introduce no new matter and read on the presently elected subject matter. Thus consideration and examination of claims 74-83 at this juncture is proper and is respectfully requested.

The new claims are fully supported by the originally filed Specification and Claims as follows:

- Claims 74 and 75 – Examples 4, 10 and 15 (pp. 39-40, 42-43, 45 and 46);
- Claim 76 – p. 3, Examples 6, 11 and 19 (pp. 40, 43 and 46);
- Claim 77 – Examples 7 and 12 (pp. 41, 42, 43 and 44);
- Claim 78 – Examples 7, 12 and 19 (pp. 41, 43, 44, 46 and 47);
- Claim 79 – Examples 7 and 12 (pp. 41, 42 and 43);
- Claim 80 – Example 20 (p. 47);
- Claim 81 – Example 16 (p. 46);
- Claim 82 – Examples 8 and 14 (pp. 41, 42 and 45);
- Claim 83 – Example 13 (p. 44).

Claims 1-4, 6, 10, 12, 16-18, and 65-83 are pending in the application. Reexamination and reconsideration of the application, as amended, are respectfully requested.

Claim Rejection Under 35 U.S.C. § 112:

Claims 65 and 66 were rejected under 35 U.S.C. §112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure "without the complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials." (Office Action, §9)

As Applicants have previously submitted, the specification provides adequate written description and enabling disclosure of the claimed antibodies as it describes methods for producing the antibodies and their specificity. In particular, the specification discloses a fully characterized antigen, a denatured collagen type-I (HU177 and XL313) or denatured collagen type-IV (HUIV26). See Applicants' Amendment filed August 10, 2004 at page 13. Applicants further believe that the specification provides disclosure adequate to teach one skilled in the art how to make the claimed antibodies without undue experimentation.

However, in an effort to expedite the examination process, applicants assure the Examiner that an acceptable deposit of hybridoma producing antibodies HUI77, HUIV26 and XL313 in compliance with 37 C.F.R. §§ 1.801 – 1.809 will be made before the date of payment of the issue fee for the instant application. Applicants assure the Examiner that (a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request; (b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application; (c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longer; and (d) the deposits will be replaced if they should become nonviable or non-replicable.

Since the Examiner has indicated that deposit of the hybridoma producing antibodies HUI77, HUIV26 and XL313 would satisfy the enablement requirements, upon deposit, withdrawal of the rejection of claims 65 and 66 under 35 U.S.C. § 112 is respectfully requested. Applicants wish to stipulate that the deposit of the hybridoma not constitute an admission of inadequate disclosure of antibodies HUI77, HUIV26 and XL313 in the specification.

Claim Rejections Under 35 U.S.C. § 102:

Claims 1-4, 6, 10, 12, 65 and 67-70 are rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,972,623 (the '623 patent). (Office Action, §11) Claims 1-4, 6, 10, 65 and 67-79 are rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,320,970 (the '970 patent). (Office Action, §12) These rejections are respectfully traversed.

As set forth in present Claim 1, the present invention is directed to antibody antagonists that (i) specifically bind denatured collagen, but bind to the native triple helical form of collagen with substantially reduced affinity; and (ii) inhibit angiogenesis.

The instant specification on pages 16 through 19 provides extensive description and examples of assays for selecting the antagonists of the invention. In particular, the specification emphasizes a two-step screening process of the antagonists of the present invention. In the described assay methods, candidate antagonists are first evaluated for their ability to selectively bind denatured collagen and then they are screened for their potency in inhibiting angiogenesis (page 16, lines 24-27). Accordingly, the claimed antibodies are required to have two properties: (1) specific affinity to denatured collagen ("specifically binds to a denatured collagen or collagens but binds to the native triple helical form of each of said collagens with substantially reduced affinity") and (2) anti-angiogenic activity ("inhibits angiogenesis").

None of the references relied upon in the art rejections suggests, much less discloses, antibodies that inhibit angiogenesis. The Official Action appears to allege that the '623 patent and the '970 patent anticipate the present claims based on inherency. It appears that the Examiner is taking the position that "inhibition of angiogenesis" is an inherent characteristic of antibodies purportedly disclosed in the '623 and '970 patents. It is respectfully submitted that the Official Action fails

to meet the burden of proof required by the Patent Office for a rejection based on inherency as set forth in MPEP § 2112.

In setting the burden that must be met in a rejection based on anticipation by inherency the Patent Office provides the following guidance:

> IV. EXAMINER MUST PROVIDE RATIONALE OR EVIDENCE TENDING TO SHOW INHERENCY
> The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. In re Rijckaert, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); In re Oelrich, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " In re Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted)
> "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original) (See www.uspto.gov/web/offices/pac/mpep/documents/2100_2112.htm#sect2112)

Here the Official Action provides no rationale or evidence to show that the antibodies disclosed in the '623 and '970 patents inherently inhibit angiogenesis.

The Official Action offers no evidence or reasoning to show that angiogenesis inhibition is a necessary property of the antibodies disclosed in the '623 and '970 patents. The Official Action provides no basis in fact or technical reasoning to reasonably support the determination that angiogenesis inhibition necessarily flows from the teachings of the cited references. As explained above, the claimed antibodies were isolated as a result of a two-step process that requires screening for both (1) specific affinity to denatured collagen and (2) anti-angiogenic activity. The cited references describe only the first part of the screening process – finding antibodies that bind to denatured collagen with higher affinity than to the helical form of collagen. There is nothing in either specification that would have directed those skilled in the art to proceed with an additional step of screening for antibodies having an anti-angiogenic activity.

The Official Action merely asserts that the antibodies disclosed in the '623 and '970 patents have the same binding specificity of monoclonal antibodies HUI77 and XL313. This assertion does not satisfy the burden set forth in MPEP § 2112 for showing that the antibodies disclosed in the '623 and '970 patents inherently possess anti-angiogenic characteristics. The apparent attempt to shift the burden to Applicants is improper and the rejection should be withdrawn.

Accordingly, claim 1 and its dependent claims 2-4, 6, 10, 12, 65 and 67-79 are patentable over the '623 patent and the '970 patent.

Claim Rejection Under 35 U.S.C. § 103:

Claims 1-4, 6, 10, 12, 16-18, 65, and 67-73 are rejected under 35 U.S.C. §103(a) as being unpatentable over the '623 patent, in view of U.S. Patent No. 5,530,101 (the '101 patent). (Office Action, §14) Claims 1-4, 6, 10, 16-18, 65, 67-69 and 71-73 are rejected under 35 U.S.C. §103(a) as being unpatentable over the '970

patent in view of the '101 patent and the '623 patent. (Office Action, §15) This rejection is respectfully traversed.

Claim 1 and its dependent claims 2-4, 6, 10, 12, 16-18, and 65-73 are patentable over the '623 and '970 patents. The '101 patent does not cure the deficiencies of the '623 and '970 patents and is not relied on by the Examiner for such. The Examiner cites the '101 patent for describing "a method of producing humanized antibodies, polypeptide fragments comprising only a portion of the primary antibody structure and a variety of cytoxic agents combined with antibodies." (Office Action, §11) Like the '623 and '970 patents, the '101 patent does not suggest or disclose antagonists that exhibit either i) a specificity to denatured collagen, or ii) anti-angiogenic properties. Therefore, claim 1 and its dependent claims 2-4, 6, 10, 12, 16-18, 65 and 67-73 are patentable over the '623, '970, and '101 patents either alone or in a combination.

New claims 74-83 are believed to be free of the rejections of record, based at least in part on the comments provided above. Accordingly, allowance of claims 74-83 is earnestly solicited.

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles, California telephone number (213) 337-6853 to discuss the steps necessary for placing the application in condition for allowance.

If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-1314.

Respectfully submitted,
HOGAN & HARTSON L.L.P.

Date: February 8, 2005

By: Olga Berson

Olga Berson, Ph.D.
Registration No. 55,001
Attorney for Applicants

Biltmore Tower
500 South Grand Avenue
Suite 1900
Los Angeles, California 90071
Telephone: 213-337-6700
Fax: 213-337-6701